The many ways of regulating biobanks

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Abstract

The collection of human biological material is an old practice that has gained new significance in the post-genomic era with the emergence of so-called „biobanks". In many academic debates and legal developments, biobanks are conceptualised as a challenge for governance. In this paper, I present the modes of governance of three biobanks therewith showing that the practice of biobanking, formerly a side-activity of biomedical research, is today on its way to become a profession of its own right, with its own ethical standards and ways of regulating. Moreover, issues related to the practice of biobanking are negotiated in regulatory processes, which can be differentiated in the following categories: professional, administrative, industrial, and public.

1. Introduction: the new significance of an old concept

The collection of biological material and associated data, also referred to as "biobanking", is far from being a new concept (Cambon-Thomsen 2004; Hansson & Levin 2003: 12f.) as biological material has been collected ever since. Biomedical research, for instance, has a long tradition of handling and managing body material both for research and therapy (Strasser 2006; Lindberg 2003; Hirtzlin et al. 2003; Holm & Bennett 2001; Hilgartner 1995). Yet, its significance is indeed "new", insofar as the organised collection of human samples in connection with the facilities of computerization of personal data poses new ethical, legal, social and political challenges, and, as Nik Brown and Andrew Webster (Brown & Webster 2004) have

phrased it, "reorders life" of the decomposed body. Thus, the significance of biobanks is (re)articulated by new management tools (such as computers and databases), scale, but also the nature of the collected material (genes and cells), and calls for new modes of governance (see also Mayrhofer 2007).

On a global level, the "biobank"-concept has no commonly agreed definition, and its meaning is articulated differently within different settings. Using the words of Anne Cambon-Thomsen, "[b]iobanks come in many different forms, according to the type of samples that are stored in the domain in which they are collected." (2004, 866), and take shape in clinical, forensic, or research settings. Sometimes, biobanks prefer to call themselves "project",[1] "laboratory",[2] "network",[3] "tumorothèque",[4] "study",[5] or "biological resource centre"[6]. These are terms that often carry no reference to biobanking at all. The OECD, for instance, adhered with its initiative on Biological Resource Centres (BRCs) to the demand of scientists for high quality stored biological resources and defines BRCs as "essential part[s] of the infrastructure underpinning life sciences and biotechnology" (OECD 2001, 11).

Initiatives like the OECD's BRC concept show that biobanks have become a major issue for the life sciences and biotechnology today. Nonetheless, only little is known - even today - about how many samples are stored by whom for which purposes.[7] This is, because, until recently, biobanking was conceived as a (archival) side activity to clinical or research activities, has become known word-of-mouth to others, and has been perceived as bio-politically insignificant. Concurrently, even those who pursue biobanking are frequently unaware of their „colleagues". For this consider the following typical statement of a French biobanker:

> Well, in this hospital complex I know of 3, no 4 biobanks ...but there could be more. All you need is a fridge, isn't it?... and over the years stuff is gathered, you know... and then genetics made a lot... well transformed as one can say a personal hobby into a biobank, you see?!

According to a memorandum by the UK's Medical Research Council, most existing collections of biological material worldwide „are too small to allow statistically meaningful research" (Council 2000) and have stimulated the emergence of a

plethora of biobank formats. A frequent distinction simply distinguishes the population-based biobank format from a disease-specific biobank format. Both formats fall under the category of research biobanks. Karen Maschke (Maschke 2005), for instance, discriminates among research biobanks between national population-based biobanks (such as the Estonian Genome Project), provincial biobanks (such as the NUgene Project of the Northwestern University, Chicago, Illinois), disease specific hospitals (such as an Alzheimer Genebank sponsored jointly by the US National Institute on Aging and the Alzheimer's Association). Also, there are biobanks that study race (such as the African Diaspora Biobank), twins (such as the GenomEUtwin) or providing anthropological information (such as the Genographic Project). Others, such as Rebulla et al. 2007 make a distinction between „leftover tissue biobanks" (devoted to the prospective banking of leftover normal and pathological tissues collected during routine clinical pathology diagnostic procedures, and „genetic biobanks" (subsuming under this category population biobanks, twin biobanks, disease biobanks, and organ biobanks). Studying population-based biobanks more in detail, Anthony Mark Cutter and Sarah Wilson (Cutter & Wilson 2004) have used different modes of governance, rather than the specimens collected or the purpose, as categories for comparison and therefore they distinguish between: (1) legislatively created/legislatively regulated (e.g. Icelandic project); (2) self-created/self-regulated (e.g. UK Biobank) and others even suggest to use the sample-size as defining category.

Large-scale biobanks, such as UK Biobank, attract most of the public and academic attention, particularly in relation to issues of informed consent and data protection (Knoppers 2005; Hoeyer 2009; Godard et al. 2003), and worldwide biobank hype could be observed since the late nineties. However, those large-scale biobanks represent only one category of a broad variety of worldwide biobank initiatives that differ in scale (number of material), regulatory framework (usually governed by a set of regulations or best practice protocols rather than an explicit law), mission goals (such as gene mapping, drug development, service institution for research teams), material (such as blood, cancer tissue, tissue slides in pathologies, bacterial strains, therapeutic substances or DNA) and operators (such as the pharmaceutical industry, patient organizations, hospitals, research groups).

Stating that current research neglects the majority of worldwide biobank initiatives studying almost exclusively on large-scale population biobanks, I looked at the modes of governance of three small scale biobanks in France in a comparative manner[8]: . the Généthon DNA and Cell Bank, the Hospital Saint-Louis Tumour Bank and the Biobanque de Picardie. Why did I select precisely those three? All three selected cases share the self-reference as "biobanks", "biological resource centres", and "service providers". Thus, they differentiate in how they make sense of their work and create meaning of their particular practice of collecting biological material. Furthermore, they differentiate in their mission goals, operators and historic origin, and provide good examples for the variety of existing biobanks and the many ways how biobanks are regulated. All biobanks are situated inside France[9], which allows framing them in a specific regulatory regime as well as social and historical context and compare their modes of governance.

2. Biobanks as a challenge for governance: three cases

In many academic debates and legal developments, biobanks are conceptualised as a challenge for governance (Gottweis & Petersen 2008; Bovenberg 2005; Cutter & Wilson 2004; Tutton 2007). One important aspect of the concept of governance is that the state is no longer in the centre of decision-making, a process that is more and more negotiated by a wide range of actors (Rose 1999, 17). Nonetheless, governance does not mean the absence of regulation or a powerful regulator. However, it refers to the negotiation process of what is established as a commonly accepted practice („the way to do things"). This can be described as a conceptual shift from „government" to „governance" (Gottweis 2008). In order to understand how this shift to governance, the concept of „ways of regulating" (Gaudillière & Hess 2009) proves useful. Four types of „ways of regulating" are to be differentiated: (a) professional regulation, (b) administrative regulation, (c) industrial regulation and (d) public regulation. Each type is characterized by different aims, actors, procedures of evidence, and regulatory tools. These tools should not be taken as fixed entities, but as categories that allow thinking about and choosing for an organising practice. After recapitulating the core activities of the three biobank case studies, these four types

shall allow me to draw general conclusions on the practice of biobanking pursued by the three cases. The concept demonstrates that various ways of regulating influence and shape biobanks. I recall, regulation is hereby defined not only to include laws and governmental degrees but also best practice protocols, harmonisation and standardisation attempts and the inclusion of the media.

The AFM's Généthon DNA and Cell Bank

Institutionally, the Généthon DNA and Cell Bank is part of Généthon, which develops therapeutic products for the treatment of rare diseases and is also involved in gene therapy and is mainly funded by the AFM (98%). The biobank is located in the Généthon building in Evry, in the same complex as the AFM itself, just a few kilometres outside Paris. Samples are provided by persons suffering a rare genetic disease as well as by their family members. The sample donor has no contact with the biobank since the samples are provided through an intermediary such as a medical doctor. After an administrative procedure (data generation and coding), samples can be processed and stored in four forms: extracted DNA, total RNA, purified lymphocytes and established lympholastoid B lines. The procedure is very clear structured and follows a strict routine followed by designated staff.

The Généthon DNA and Cell Bank remains, through Généthon, under the decision-making powers of the AFM. The Généthon DNA and Cell Bank's mission is to collect, prepare, store and distribute DNA from rare genetic disorder patients and their family members. The goal is to be a service provider of biological material for research teams. Material is handed over to the research teams only if their research project holds a potential for the benefit of rare genetic disease patients.

Thus, the biobank's activities are articulated by the practices and discourse of the patient organization AFM and are embedded in the context of biomedical research. Although a service institution for research teams, the staff sees the daily work for the benefit of the rare disease patients and refers to the samples as „immortalised sick persons", stressing that the samples will „outlive their donors", and describing the biobank as a space, a territory where rare disease patients (or more precisely their samples) can reach over time a significant mass or size. Size is a major issue for the

patient organisation; Knowledge about rare diseases is difficult to gain as a significant size of sample is hardly assembled by a single researcher but only in a joint effort. Consequently, the biobank is highly interconnected with other rare disease biobanks on the European level (e.g. EuroBioBank) and advocates a positive image of rare disease patients as warriors having taken their fate in their own hands. Especially the biobank's website, but also the Téléthon (a yearly fund raising festival) transport a positive message about the practice of biobanking as a meaningful pursuit.

The Biobanque de Picardie

The Biobanque de Picardie is an association *à but non lucratif* (loi de 1901) receiving financial support from the Conseil Régional de la Somme, the region of Picardie, Amiens Métropole, the Université Jules Verne à Amiens, and the CHU d'Amiens. Additionally, the biobank has received financial support from the Ministry of Research and the FEDER for the acquisition of new cryopreservation equipments. It focuses on scientific projects interested in infectious diseases (HIV, hepatitis C). The bank collaborates with a wide range of research teams (from universities as well as from the pharmaceutical industry) on fundamental and applied research projects. The biobank participates in both prospective and retrospective epidemiological surveys with public and private sector partners. Also, it participates in fundamental and applied research projects in collaboration with hospitals, universities or private companies (e.g., conception and development of new diagnostic tools for infectious diseases). It is a member of the International Society for Biological and Environmental Repositories (ISBER) and the Marble Arch Group (a think tank on biobank related issues).

The biobank's staff is highly informed on recent developments in the field, especially new guidelines. By October 2008, the biobank contained 8000 samples stored in electric freezers at -80°C or in liquid nitrogen at -196°C. In its conception and organisation, the biobank is open to all potential users. For example, it stores a collection of the WHO on contractual basis. Also, its services are not only restricted to human samples: upon request it stores the DNA of the famous horses of the region Picardie. All staff is paid by the overall budget of the CHU. It is envisioned that

the Biobank the Picardie shall centrally store all collections of the CHU. This vision is facing resistance from those who have initiated the collections in the first place. The biobank also runs a website that informs potential „customers" about the history and services of the biobank. Overall, the biobank employs a start-up narrative.

The Hospital Saint-Louis Tumour Bank

The Hospital Saint-Louis Tumour Bank is one of many biobanks located at the Saint-Louis hospital and is associated to its pathology institute. In comparison to other biobanks in a hospital setting, it disposes its own budget, explicitly included in the yearly overall budget of the hospital. However, approximately half of its activities are funded through other sources (e.g. research projects, funds). The biobank is specialized on cancer tissue, and received considerable funding over the years when the French Ministry of Research announced cancer as one of the main issues in French health care policy. Between 2001 and 2004, the biobank had successfully answered to the DHOS call and received a significant grant of 90.000 Euros. The grant was used for personnel costs and the development of a database. The biobank has 5-10 staff members, depending on who is counting. The impreciseness results of the fact that most staff members are regular employees of the clinic and carry out the tasks for the biobank as additional duties. The tumour bank is composed of samples which have been collected during clinical routine and – given informed consent was collected – are used for research. After a first macroscopic analysis, the sample is processed and stored in the tissue bank, usually shock frozen. A brochure entitled "Le Service de Pathologie. du diagnostic...à la recherche" informs the patient about the basic biobanking procedures. The biobank contains tumor samples for lymphoma, breast cancer, colonic cancer, kidney cancer, skin cancer, thyroid tumors and ucleic acids extracted from them. The INCa recommendations for tumour banks and the ethical charter on the collection, storage and use of human tumour samples for therapeutic or cancer research purposes (INCa 2005) are referenced as guidelines for the biobank's practices. Since about a decade, clinical data is linked to the samples. In 2006, the biobank contained 38470 samples and 26685 patient records. The records are kept in the database TumoroteK. that is a web application that provides the users with tools to efficiently manage their biological sample banks:

storage of materials, clinical and biological data and distribution of material. The directorate of hospitals and healthcare organisations (DHOS) of the French Ministry of Health has launched the project in 2002 within the national framework of the "Plan Cancer". At Hospital St. Louis, TumoroteK V1.01 is fully operational since December 2004.

Also in the same year, the Institut National du Cancer (INCa) commissioned a task force to conduct a survey on French tumour banks. The survey reveals a significant number of tumour banks in many university hospitals and cancer centres. The survey concluded that two factors limit the scientific value of cryo-preserved samples and collections: the lack of paucity of clinical data and the low proportion of patients who have provided consent for the use of their samples in biomedical research. The biobank participates in several research projects. Users of the samples seem to be a rather closed club: mostly those physicians who have invested their time in collecting the samples (and/or their research collaborators) are also the users. A clear access policy to the tissue bank for „outsiders" is in transparent. The activities of the biobank are reasoned as amelioration for healthcare and a better combination of clinical routine and research. The biobank staff and associated researchers are highly active in working groups for best practice guidelines for the practice of tissue banking.

3. Comparing ways of regulating

The three case studies presented in this paper show that the practice of biobanking, formerly a side-activity of clinical or research activities, is today on its way to become a profession of its own right, with its own ethical standards and modes of governance. While biological material is increasingly seen as crucial resource for biomedical research, a wide range of risks, such as infringement of genetic privacy and of data protection, associated with the processing, storing and exchanging of material and data, has been diagnosed and discussed by many academic scholars and legal experts. Often, these risks are tackled by soft rules and regulations addressed by both ELSI experts and biobank practitioners rather than a tight set of laws. Biobankers employ a pragmatic way of self-governance for the sake of their

scientific objectives and the reputation of their own institution (Mayrhofer & Prainsack 2009). Moreover, the issues related to the practice of biobanking are negotiated in regulatory processes, which can be differentiated in the following categories: professional, administrative, industrial, and public.

Professional governance stems from biobanking societies, public health authorities, networks of biobanks, expert committees (such as the one drafting the INCa guidelines) and ELSI-experts. It includes the processes that it takes to reach a consensus on good practices and guidelines. Biobankers, both in France and internationally, often employed these ways of regulating in the absence of a consistent legal framework but also to address issues and risks that so far have not been a concern of state regulation. Certainly, technological and scientific progress progresses much faster than state regulation can follow. Consequently, these guidelines become an integral and essential part of professional regulation.

Once good practice guidelines become approved and henceforth a governing institution (such as a public hospital) commits to the adherence of such guidelines, then guidelines can also become part of the administrative way of regulating. This, since the implementation of guidelines requires agencies and control mechanisms that enforce them. In addition, administrative regulation includes the implementation of rigid procedures on informed consent, database validation, MoUs and contracts, or approval of a research project by the ministry of research and ethics committees.

Another way of regulating is industrial regulation. Rather than having the industry in the centre, industrial regulation talks about the way regulation is tackled. In other words, it talks about the way how material is collected, processed, registered, and distributed. Industrial regulation refers to quality control and standardisation. Therewith, it is not important whether the regulation is imposed by a central regulator, and agency or a customer (which might be a pharmaceutical company). In case of the Biobanque de Picardie, quality is a major concern. This, because the biobank offers services to pharmaceutical industry that they require standardised data and high quality samples for statistically meaningful results.

The last way of regulating concerns public regulation which is associated with the self-empowerment of patients „either in isolation or as members of civil society organisations and/or social movements" (Gaudillière & Hess 2009, 12). Also, biobanks aim at directly shaping their public image and appearance of which the web access of biobanks provides telling examples. Often directed to address the general public and professionals in the field (future customers, researchers), these websites provide an arena for biobankers to talk about their practices, services but also take a stand on their values. Exemplarily, the Généthon DNA and Cell Bank uses the website to promote its activities to its supporters. Therein it reflects the proclaimed values and goals of its governing institution, the Généthon and the patient organisation AFM. Certainly public regulation also includes media perception, parliamentary debate or the opinion of the CCNE on biobanks. These social worlds, however, can be put aside in my elaborations since biobanking did not raise a wide public debate.

Whereas the professional way of regulating is guided by the values of an entire profession and their work ethics and competency, administrative regulation is generally guided by concerns of public health and the protection of the institution (contracts) or the individual (data protection). Industrial regulation is heavily guided by the aim for profit, productivity, and efficacy. Lastly, the public way of regulating pays reference to all bioethical considerations and calls for transparency.

Biobanks are a new phenomenon which do not yet have well established sites, practices, modes of operation, governance and supervision, developing the right „tools" (such as how to store and process the data; whom – and how – to grant access; how to enforce informed consent, etc) is often as much part of the project as the objectives for which the tools are developed (see also Ratto 2006).

The practice of biobanking, formerly a side-activity of clinical or research activities, is today on its way to become a profession of its own right, with its own ethical standards and modes of governance, implying a high level of organisation and explicit rules. Additionally, biobanking master courses are offered by several universities, such as the University of Picardie.

These developments often remain invisible for the biobanker's own environment, especially in the clinical context, where the biobanker's work might not be depicted as „scientific". For the biobanker, biobanking organisations (such as P3G) or international conferences (such as ESF 2009) are perceived as a manifestation of the changed recognition, the professionalization of the practice of biobanking, and their new ways of regulating the practice of collecting, manipulating, storing, and distributing biological material.

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Notes

[1] Such as the Estonian Genome Project, see http://www.geenivaramu.ee/index.php?show=main&lang=eng (accessed August 17, 2005).

[2] Such as the National Laboratory for the Genetics of Israeli Populations at the University of Tel Aviv, see http://www.tau.ac.il/medicine/NLGIP/nlgip.htm (accessed August 17, 2005).

[3] Such as the Singapore Tissue Network, see http://www.gis.a-star.edu.sg/homepage/gisbiodomains-tissue.jsp (accessed August 17, 2005).

[4] Such as in Bordeaux by the Direction de l'hospitalisation et de l'organisation des soins (Inserm 2005: 16).

[5] Such as the National Children's Study in the U.S., see http://nationalchildrensstudy.gov, (accessed August 17, 2005).

[6] Such as the Biological Resource Centre initiative by the OECD, see http://www.oecd.org/document/50/0,2340,en_2649_34537_1911986_1_1_1_1,00.html (accessed August 18, 2006).

[7] Several studies have attempted to count biobanks on a national or international level. Consider for instance the catalogue of European biobanks a collaborative effort of BBMRI and P3G (http://www.bbmriportal.eu). The catalogue allows queries by country, by biobank, by ICD-groups, by specimen types, etc.

[8] Methodologically, my research is grounded in a comparative case study approach, the study of documents (such as best-practice protocols or recommendations), a series of qualitative interviews and extensive on-site observations.

[9] Why France? Firstly, France neither has planned, nor is planning, to establish a large-scale national biobank, but has a broad variety of biobanking initiatives (CCNE 2003) and, therefore, is more representative of the majority of countries worldwide. Secondly, French biobanks are highly networked and their governance is based on Best Practice Protocols and the like. Thirdly, France is leading the OECD Task Force on BRCs and is highly active in biobanking issues both on the European and international level.

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